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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,904	11/21/2006	**Martin F. Bachmann**	1700.0420001/BJD	7074

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EXAMINER	
SAUNDERS, DAVID A	
ART UNIT	**PAPER NUMBER**
1644	
MAIL DATE	**DELIVERY MODE**
04/03/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/556,904	BACHMANN ET AL.	
	Examiner	Art Unit	
	David A. Saunders	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7,9,15,19,20,32,35,37,39,44,47,49,52,53,57,59,61 and 62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,9,15,19,20,32,35,37,39,44,47,49,52,53,57,59,61 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/15/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

AMENDMENT ENTRY

Amendment of 11/15/05 has been entered. Claims 1, 3-4, 7, 9, 15, 19, 20, 32, 35, 37, 39, 44, 47, 49, 52-53, 57, 59 and 61-62 are pending and are under examination.

OBJECTION(S) TO DISCLOSURE

The amendment filed 11/15/05 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The new matter is introduced by virtue of the fact that U.S. provisional Application No. 60/470,443 has been entirely incorporated by reference, since it was not incorporated by reference at the International Stage.

Applicant is required to cancel the new matter in the reply to this Office Action.

REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 3, 32, 35, 37, 39, 44, 47, 49, 53 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "virus-like" in claims 3 and 47 is a relative term which renders the claim indefinite. The term "virus-like" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The fact that claims depending from claims 3 or 47, such as claims 7 or 9, refer to a “virus-like” particle as comprising recombinant proteins or fragments thereof confuses the matter. Since the recombinant proteins are not per se a virus, even if they are engineered from a virus. Also, one does not know whether “virus-like” particles are derived from a virus or not. If all that is required is that they form some sort of “supramolecular structure built in a symmetric manner” (e.g. spec. p 6), then numerous non-viral proteins could be considered to fall within this rubric –e.g. flagellin proteins.

However, flagellin proteins are derived from bacteria, not from viruses. What then makes "virus-like" particles "virus-like"?

In claim 32, last line "a second fluorochrome" is confusing, since no "first fluorochrome" has been recited in base claim 1.

In claim 37, line 2 "a second set of at least one second additional targeting molecule" is confusing, because base claim 1 has not referred to any "first set of at least one first targeting molecule". Applicant may correct by rendering claim 37 dependent from claim 32.

Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are: that there is no stated relationship between the antigen being used in the "first composition" of base claim 1 and the antigen used in the "second composition" of claim 44. No such relationship is clearly stated until one reads further dependent claim 57 (not listed among the rejected claims).

REJECTION(S) UNDER 35 USC 112, FIRST PARAGRAPH

Claims 3, 7, 9, 47, 49 and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant has not adequately described the genus of "virus-like" particles.

Specifically, one does not know whether these particles are derived from a virus or not. If all that is required is that they form some sort of "supramolecular structure built in a symmetric manner" (e.g. spec. p 6), then numerous non-viral proteins could be considered to fall within this rubric.

Claims 1, 3-4, 7, 9, 19-20, 37, 39, 44, 47, 49, 52-53, 57, 59 and 60-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the case in which the "second labeling compound" of claim 1 serves to label "at least one first targeting molecule" (as in claim 32), does not reasonably provide enablement for the case in which the "second labeling compound" of claim 1 is non-targeted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Applicant has not disclosed any example of a "second labeling compound" that, per se, can carry out the function of "labeling B-cells in a mixture of cells", as required by step E) of claim 1. Where the labeling of B-cells is described (e.g. para spanning pp 15-16 and para spanning pp 26-27) every marker on the surface of the B-cells is something that would only be detectable with the use of a "targeting molecule", such as an antibody. Note that every one of the CD markers suggested by applicant was historically defined by monoclonal antibodies. If there is any other way of identifying the CD antigens, a "targeting molecule" would still be required (e.g. a lectin, a carbohydrate, etc.) that would function in place of the antibody originally used to define the CD antigen.

Note too, that every one of the "labeling compounds" described (e.g. at p 18) would not be capable, per se, of labeling B-cells. Even within these teachings, applicant notes that these "labeling compounds" must be linked, directly or indirectly, to an antibody, or to some other kind of specific binding member.

For the above reasons, the limitations of claim 32 are required in base claim 1, in order for claim 1 and its other dependents to be enabled.

Claims 1, 3-4, 7, 9, 19-20, 32, 35, 37, 39, 44, 47, 49, 52-53, 57, 59 and 60-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the case in which the "first labeling compound" of claim 1 serves to label "at least one first targeting molecule", does not reasonably provide enablement for

the case in which the "first labeling compound" of claim 1 is non-targeted. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

This rejection assumes that steps A)- (F) of claim 1 are conducted in order. In such case, Applicant has not disclosed any example of a "first labeling compound" that, per se, can carry out the function of "labeling said first composition", as required by step D) of claim 1. Where such labeling of the "first composition" is described (e.g. p 25, line 29-p 26 line 30), the "first labeling compound" is targeted to the "first composition" via direct or indirect labeling of and antibody specific for a component of the "first composition".

Note too, that every one of the "labeling compounds" described (e.g. at p 18) would not be capable, per se, of labeling the "first compound". Even within these teachings, applicant notes that these "labeling compounds" must be linked, directly or indirectly, to an antibody, or to some other kind of specific binding member.

If one assumes that that steps A)- (F) of claim 1 need not be conducted in order, then the only other possibility would be that the "first composition" is labeled with the "first labeling compound" prior to contacting the cells with the "first composition" (e.g. as disclosed at p 25, lines 16-28). In any event, claim 1 is overly broad because it does not specify that either i) the "first labeling compound" of step E) is targeted, directly/ indirectly, by at least one targeting antibody, or ii) that the "first composition" is labeled with the "first labeling compound" prior to contacting the cells with the "first composition".

REJECTION(S) UNDER 35 USC 103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3,-4, 7, 15, 19-20, 32, 37, 39, 44, 47, 49, 52, 57, 59 and 60-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weitkamp et al (cited in IDS of 11/15/05) in view of Renner et al (WO/00/32227 or US 7,229,624, cited on PTO-892).

Weitkamp et al has a publication date that renders it citable under 35 USC 102 (a), assuming that applicant's provisional application (60/470,443) supports every

feature of the instant clams. Weitkamp et al is citable under 35 USC 102 (b), should any feature of the instant claims not be supported by 60/470,443.

Renner et al (WO/00/32227) was cited by applicant at spec. p 50. It has a publication date that renders it citable under 35 USC 102 (b). Renner et al (US 7,229,624) is citable under 102 (e). The two Renner et al documents are of the same patent family. For convenience, the examiner shall cite only the US reference by col. And line no. The WO publication has not been supplied because it is of an unwieldy size.

Weitkamp et al shows every feature of instant claim 1, for the case in which the labeling step D) is conducted prior to step C) of contacting the cells with the "first composition" (i.e. the core particles are pre-labeled with an incorporated GFP). The only difference between the method of Weitkamp et al and the instant method is that Weitkamp et al uses "the core-particles" (comprised of RV-recombinant proteins) serve as the antigen, per se.

Renner et al ('624) show that core-particles may be used to present any bordered array of any antigens or epitopes/antigenic determinants, by attaching the antigens or determinants thereto. The attaching of the antigens or determinants to the core-particles may be effected via a "chemically reactive group" which would inherently form a "covalent bond". While Renner et al use these core particles with attached antigens or determinants to immunize, it would have been obvious that these particles would be used to identify B-cells from any immunized subject, in a manner analogous to that of Weiltkamp et al. One would have been motivated to do so for cases in which one

wanted to identify B-cells which produce antibodies against antigens other than antigens which comprises a core-particle per se (i.e. against antigens other than viral recombinant proteins).

From the above instant claims 1, 15 and 19 would have been obvious.

Regarding claims 3-4, Weitkamp et al shows core-particles that are "virus-like" by virtue of being composed of recombinant Rotavirus proteins.

Regarding claim 7, Renner et al teaches the use of core-particles/virusllke particles derived from RNA viruses, such as Sinbis virus or Alphaviruses.

Regarding claims 19-20 and 32, Weitkamp et al use dual fluorescent labels to identify antibody producing B-cells.

Regarding claims 37 and 39, Weitkamp et al stain the B-cells, indirectly, with a third fluorescent label, in order to select IgD (-) B-cells.

Regarding claim 44, 47, 49 and 57, since Renner et al teach use of core-particles/virus-like particles to immunize, it would have been obvious to have immunized an animal with these, in order to induce B-cells to be selected for the production of monoclonal antibodies.

Regarding claims 61-62, Renner et al employ methods of gentic engineering to produce an antibody having the same binding specificity as the antibody produced by the selected B-cell. Fig. 2 shows that the VH and VL segments were expressed in a fusion construct.

Regarding claim 59, the recited method of generating a hybridoma from a selected B-cell was known in the art (e.g. Weitkamp et al at p 224, col. 1). Even though

Weitkamp et al points out some disadvantages of this method, it would have been obvious to use it, if one were willing to accept these disadvantages.

Claims 9 and 52-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weitkamp et al (cited in IDS of 11/15/05) in view of Renner et al (WO/00/32227 or US 7,229,624), as applied to claims 1, 3, 44 and 47 above, and further in view of either or both of Vasiljeva et al and Fehr et al (both cited in IDS of 11/15/05).

Each tertiary reference shows the use of a Q-beta bacteriophage as a core-particle/virus-like particle for presenting an ordered repetitive array of antigens or antigen determinants/epitopes. These references teach that these particular particles can be advantageous for presenting the determinants with the correct spacing distances between the determinants for inducing B-cell responses. It thus certainly would have bee obvious to use such particles in the immunizing steps of instant claim 44. Since one would have expected these particles to function in a manner equivalent to the RV virus-like particles of Weitkamp et al, it would have also been obvious to use Q-beta bacteriophage particles in a method analogous to that of Weitkamp et al for detecting and selecting B-cells.

Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weitkamp et al (cited in IDS of 11/15/05) in view of Renner et al (WO/00/32227 or US 7,229,624, cited on PTO-892) as applied to claims 1 and 32 above, and further in view of Chang (5,326,696, cited in IDS of 11/15/05).

Chang shows that there are numerous B-cell surface markers, other than the CD19 marker employed by Weitkamp et al that may be used to identify dual stained B-cells that produce antibodies specific for an antigen. One of these alternative markers is cell surface IgG, and it is detected with a targeting molecule that is F(ab')2 (e.g. claim 4 of Chang).

CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara, can be reached on 571-272-0878. The fax phone number for the organization where this application is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 3/3/0/09 DAS

/David A Saunders/

Primary Examiner, Art Unit 1644